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Persistent photoperiodic effects on immunological responsiveness: shedding light on immunity

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A COMPETENT IMMUNE SYSTEM is crucial for maintaining a sufficiently high level of disease resistance. Immunity, however, is a double-edged sword. Impaired immunity increases susceptibility to pathogens and can increase the likelihood of sickness or death. Excessively heightened immune responses, in which our immune system fails to distinguish "self" from "non-self" or responds in excess to a benign substance, may be equally debilitating and can lead to a host of allergies and autoimmune diseases. Thus it is important to maintain an "optimal level" of immune responsiveness to maximize disease resistance. Immunity, however, is not a static process; marked seasonal fluctuations in immune function and subsequent disease resistance exist in a wide range of species, including humans (5, 7, 8, 12). Although much progress has been made over the last decade in our understanding of how the immune system works, considerable gaps in our knowledge persist, especially in terms of naturally occurring, environmentally influenced fluctuations in immune function and disease resistance. A wide variety of infectious diseases (e.g., AIDS, malaria, influenza) display pronounced seasonal fluctuations (8). Although some of this variation is undoubtedly due to seasonal fluctuations in pathogen prevalence, seasonal changes in host immunity likely contribute to seasonal changes in disease as well. The majority of studies investigating seasonal changes in disease, however, has focused on monitoring pathogen prevalence; we are only just beginning to understand the physiological mechanisms underlying seasonal changes in host immune function.

Over the last decade, studies in a variety of mammalian and nonmammalian species have demonstrated that seasonal changes in both humoral and cell-mediated immune function are under environmental control and are mediated predominantly by changes in the ambient photoperiod (day length) (1–4, 6, 11). Although the effects of changes in day length on immune function are now reasonably well documented (7, 8), an important question remains: are photoperiodic changes in immunity transient responses to the prevailing day length or do they represent long-lasting changes in the immune system that could have important ramifications for subsequent immune surveillance? The study presented by Prendergast et al. (9) in this issue of *American Journal of Physiology-Regulatory, Integrative and Comparative Physiology* provides an important initial step in addressing this very question. These researchers and others have previously documented photoperiodic changes in immunity in seasonally breeding Siberian hamsters. Specifically, hamsters housed in short "winterlike" day lengths display reduced humoral immunity but increased delayed-type hypersensitivity (DTH) compared with animals housed in long, "summerlike" photoperiods (3, 10, 11). The experiments reported here by Prendergast et al. tested the effects of prior photoperiodic exposure on subsequent immune responsiveness. Specifically, the authors examined whether day length exerts its effects on secondary antibody and delayed-type hypersensitivity (DTH) responses by affecting immunity only during primary exposure or whether initial exposure to long or short days would have persistent effects on immunity when animals were reexposed to the same antigens under differing photoperiodic regimes.

As expected, exposure to short day lengths decreased both primary and secondary antibody responses to the antigen keyhole limpet hemocyananin (KLH) and increased DTH responses to the chemical antigen DNFB. DTH reactions, however, were not only affected by the ambient photoperiod, but also by the previous photoperiod in which the animals had been initially inoculated ≥8 wk before their subsequent testing. In other words, short-day enhancement of DTH responses persisted even when animals were subsequently transferred to long days and retested with the same antigen. Thus exposure to short days not only affects the initial immune response per se, but also influences the establishment of an immunological memory of the response as well. Collectively, these data suggest that exposure to pathogens during short day lengths can have enduring consequences for subsequent immune responses to similar pathogens. Because most species, including humans, are likely to encounter a particular pathogen repeatedly over the course of their lifetimes, these long-lasting immunological effects have the potential to alter an animal's subsequent ability to resist seasonally recurring diseases to which it may be reexposed. As the authors suggest, these data are consistent with the notion that exposure to specific day lengths can regulate the formation, retention, and subsequent retrieval of antigen-specific immunological memory. More broadly, these results demonstrate that environmental factors such as day length, in addition to their immediate influences on physiological responses, can exert profound, long-lasting effects on the immune system, presumably through their actions on immunological memory. These environmental influences would likely have significant repercussions on subsequent immune surveillance and disease resistance and thus affect host survival.

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REFERENCES

1. **Brainard GC, Knobler RL, Podolin PL, Lavasa M, and Lubin FD.** Neuroimmunology: modulation of the hamster immune system by photoperiod. *Life Sci* 40: 1319–1326, 1987.
2. **Champney TH and McMurray DN.** Spleen morphology and lymphoproliferative activity in short photoperiod exposed hamsters. In: *Role of Melatonin and Pineal Peptides in Neuroimmunomodulation*, edited by Franchini F and Reiter RJ. New York: Plenum, 1991.
3. **Demas GE, Drazen DL, Jasnow AJ, Bartness TJ, and Nelson RJ.** Sympathoadrenal system differentially affects photoperiodic changes in immune function in Siberian hamsters (*Phodopus sungorus*). *J Neuroendocrinol* 14: 29–35, 2002.

4. **Demas GE and Nelson RJ.** Photoperiod and ambient temperature interact to affect immune parameters in male deer mice (*Peromyscus maniculatus*). *J Biol Rhythms* 11: 95–103, 1996.
5. **Dowell SF.** Seasonal variation in host susceptibility and cycles of certain infectious diseases. *Emerg Infect Dis* 7: 369–374, 2001.
6. **Drazen DL, Kriegsfeld LJ, Schneider JE, and Nelson RJ.** Leptin, but not immune function, is linked to reproductive responsiveness to photoperiod. *Am J Physiol Regul Integr Comp Physiol* 278: R1401–R1407, 2000.
7. **Nelson RJ and Demas GE.** Seasonal changes in immune function. *Q Rev Biol* 71: 511–548, 1996.
8. **Nelson RJ, Demas GE, Klein SL, and Kriegsfeld LJ.** *Seasonal Patterns of Stress, Immune Function and Disease.* Cambridge, UK: Cambridge University Press, 2002.
9. **Prendergast BJ, Bilbo SD, and Nelson RJ.** Photoperiod controls the induction, retention, and retrieval of antigen-specific immunological memory. *Am J Physiol Regul Integr Comp Physiol* 286: R54–R60, 2004.
10. **Prendergast BJ, Yellon SM, Tran LT, Nelson RJ.** Photoperiod modulates the inhibitory effect of in vitro melatonin on lymphocyte proliferation in female Siberian hamsters. *J Biol Rhythms* 16: 224–33, 2001.
11. **Yellon SM, Teasley LA, Fagoaga OR, Nguyen HC, Truong HN, and Nehlsen-Cannarella L.** Role of photoperiod and the pineal gland in T cell-dependent humoral immune reactivity in the Siberian hamster. *J Pineal Res* 27: 243–248, 1999.
12. **Zapata AG, Varas A, and Torroba M.** Seasonal variations in the immune system of lower vertebrates. *Immunol Today* 13: 142–147, 1992.